Complete Summary

GUIDELINE TITLE

ASGE guideline: the management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures.

BIBLIOGRAPHIC SOURCE(S)

Zuckerman MJ, Hirota WK, Adler DG, Davila RE, Jacobson BC, Leighton JA, Qureshi WA, Rajan E, Hambrick RD, Fanelli RD, Baron TH, Faigel DO. ASGE guideline: the management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures. Gastrointest Endosc 2005 Feb;61(2):189-94. [56 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Diseases or conditions requiring gastrointestinal endoscopy in patients with concomitant cardiovascular conditions requiring low molecular weight heparin (LMWH) or nonaspirin antiplatelet agents

GUIDELINE CATEGORY

Management
Prevention
Risk Assessment

CLINICAL SPECIALTY

Gastroenterology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To address the management of patients undergoing endoscopic procedures who are on either anticoagulation therapy with low-molecular-weight heparin (LMWH) or clopidogrel and other new antiplatelet therapies, including glycoprotein (GP) IIb/IIIa inhibitors

TARGET POPULATION

Patients undergoing endoscopic procedures who are on either anticoagulation therapy with low-molecular-weight heparin (LMWH) or clopidogrel and other new antiplatelet therapies, including glycoprotein (GP) Iib/IIIa inhibitors

Note: This guideline does not address the management of patients who are on warfarin and unfractionated heparin (UFH) therapy, as well as aspirin and other nonsteroidal anti-inflammatory drugs. Another guideline addresses this population of patients.

INTERVENTIONS AND PRACTICES CONSIDERED

Management of Anticoagulation/Antiplatelet Therapies

1. Weighing the benefits and risks of stopping therapy
2. Reversing or stopping therapy, including use of intravenous protamine sulfate for quick reversal of effects of low-molecular weight heparin (LMWH) and platelet transfusion for quick reversal of effects of clopidogrel or ticlopidine
3. Continuing therapy
4. LMWH as bridge therapy for warfarin
5. Restarting LMWH or non-aspirin antiplatelet agents

MAJOR OUTCOMES CONSIDERED

- Risk of bleeding related to endoscopic procedures and/or use of low molecular weight heparin (LMWH) or nonaspirin antiplatelet drugs
- Risk of thromboembolic complications in the absence of antiplatelet agents
- Efficacy of low molecular weight heparin (LMWH) and nonaspirin antiplatelet drugs in the prevention and the treatment of thromboembolic disease
- Cost-effectiveness of approaches to managing periprocedure anticoagulation

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

In preparing this guideline, a MEDLINE literature search was performed, and additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. Prospective controlled trials
B. Observational studies
C. Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Guidelines for the appropriate practice of endoscopy are based on critical review of the available data and expert consensus.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Published cost analyses were reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Levels of Evidence A-C are defined at the end of the "Major Recommendations" field.

Low Molecular Weight Heparin (LMWH)

There are no published studies on the use of low molecular weight heparin (LMWH) in patients undergoing endoscopy. Despite this lack of data, the clinical use of these agents in patients undergoing endoscopy probably should follow analyses indicating the most cost-effective approach to managing periprocedure anticoagulation.

1. Acute gastrointestinal (GI) hemorrhage in the patient taking low molecular weight heparin (LMWH).

   The decision to reverse or to stop this therapy, risking an adverse ischemic event or a thromboembolic complication, must be weighed against the risk of continued bleeding by maintaining continued systemic anticoagulation. Because of the short half-life of the LMWHs, the anticoagulant effect may be reversed within 8 hours of the last dose. If quick reversal is required, intravenous protamine sulfate can be used. Note that the administration of protamine sulfate can cause severe hypotension and anaphylactoid reactions.

2. Elective endoscopic procedures in the patient taking LMWH.

   A decision regarding discontinuation of therapy before endoscopy has to be weighed against the patient's risk for developing an adverse ischemic event or thromboembolic complication. Endoscopic procedures have been previously categorized as low or high risk for bleeding (see Table below). Low- or high-risk clinical conditions for thromboembolic complications also have been previously defined.

   Low-risk Procedures

No adjustments in anticoagulation need be made, irrespective of the underlying condition.

High-risk Procedures

Discontinue LMWH at least 8 hours before the anticipated therapeutic endoscopy. The decision as to when to restart therapy should be individualized.

Table. Management of Low-molecular-weight Heparin (LMWH) and Nonaspirin Antiplatelet Agents for Endoscopic Procedures

Management of LMWH in patients undergoing endoscopic procedures

Procedure risk	Recommendation
High	Consider discontinuation at least 8 hours before procedure
Low	No change in therapy

Reinstitution of LMWH should be individualized.

Management of antiplatelet medication (clopidogrel or ticlopidine) in patients undergoing endoscopic procedures

Procedure risk	Recommendation
High	Consider discontinuation 7 to 10 days before procedure
Low	No change in therapy

Patients on combination therapy (e.g., clopidogrel and aspirin) may be at an additional increased risk of bleeding.

For acute GI hemorrhage in the patient on clopidogrel or ticlopidine, the decision to transfuse platelets should be individualized, usually weighing the risk of an acute cardiovascular event against the risk of continued bleeding.

Reinstitution of clopidogrel or ticlopidine should be individualized.

Procedure risk

High-risk procedures	Low-risk procedures
Polypectomy	Diagnostic
Biliary sphincterotomy	EGD ± biopsy
Pneumatic or bougie dilation	Flexible sphincterotomy ± biopsy
PEG placement	Colonoscopy ± biopsy
EUS-guided FNA	ERCP without endoscopic sphincterotomy
	Biliary/pancreatic stent without endoscopic

Laser ablation and coagulation Treatment of varices	sphincterotomy EUS without FNA Enteroscopy

Abbreviations: PEG = percutaneous endoscopic gastrostomy, EUS = endoscopic ultrasound guided, FNA = fine needle aspiration, ERCP = endoscopic retrograde cholangiopancreatography, EGD = esophagogastroduodenoscopy, LMWH = low molecular weight heparin

3. Elective endoscopic procedure in the patient taking warfarin who may need bridge therapy.

   LMWH may be useful in extending the period of systemic anticoagulation while the effects of long-acting warfarin are allowed to dissipate. LMWH may replace the previous standard of a "heparin window" in high-risk patients. Considerations in favor of LMWH would be the enhanced quality of life for the patient (i.e., no therapeutic monitoring, avoidance of hospitalization, no need for intravenous access) and the possible economic savings of outpatient LMWH compared with a hospital-based "heparin window." LMWH should not be used in pregnant women with mechanical prosthetic heart valves. In non-pregnant patients with mechanical valves, short-term use appears to be safe but prospective controlled data are lacking.

   Low-risk Procedure

   No adjustments in anticoagulation need be made, irrespective of the underlying condition.

   High-risk Procedure

   Discontinue warfarin three to five days before the procedure and concomitantly begin administering LMWH. Consider using dose ranges as for the treatment of patients with acute deep venous thrombosis (DVT) (e.g., enoxaparin 1 mg/kg subcutaneously every 12 hours). Discontinue LMWH for at least eight hours before the therapeutic endoscopy. The decision as to when to restart therapy should be individualized.

Non-Aspirin Antiplatelet Agents

There are no published studies regarding the safety of endoscopic procedures in the setting of these antiplatelet agents. The following recommendations are based on their pharmacology and known clinical effects.

1. Acute GI hemorrhage in the patient taking clopidogrel or ticlopidine.

   Clopidogrel or ticlopidine should be discontinued. The decision to reverse the antiplatelet effect, risking ischemic consequences, must be weighed against the risk of continued bleeding by maintaining the state of impaired platelet aggregation. If quick reversal is required, platelet transfusion may be appropriate.

2. Elective endoscopic procedures in the patient taking clopidogrel or ticlopidine.

   A decision regarding discontinuation of therapy before endoscopy has to be weighed against the patient's risk for developing an adverse ischemic event, including coronary stent occlusion. Endoscopic procedures previously have been categorized as low risk or high risk for bleeding (see Table above).

   Low-risk Procedures

   No adjustments in the antiplatelet regimen need to be made.

   High-risk Procedures

   Whether to discontinue these agents has not been determined. If discontinued, they should be stopped seven to ten days before the procedure. Because of the slow onset of action, it may be appropriate to restart the drug the following day. In patients who receive clopidogrel plus aspirin, consider reversion to a single agent (preferably aspirin) before elective endoscopy.

3. Patients taking dipyridamole.

   In the absence of a preexisting bleeding disorder, endoscopic procedures may be performed in patients who take dipyridamole or combination dipyridamole-aspirin in standard doses. However, the safety in patients undergoing high-risk procedures is unknown.

4. Patients taking a GP IIb/IIIa inhibitor.

   Patients being considered for elective endoscopy are not typically exposed to this class of drug. For patients requiring emergency endoscopy for acute GI hemorrhage, the GP IIb/IIIa infusion should be discontinued. Eptifibatide and tirofiban have a relatively short duration, of about four hours of action, whereas abciximab may last up to 24 hours. Transfusion of platelets or use of desmopressin (DDAVP) may play a role in the setting of major bleeding.

Summary

Levels of Evidence A-C are defined at the end of the "Major Recommendations" field.

- LMWH and non-aspirin antiplatelet drugs are effective in the prevention and the treatment of thromboembolic disease. (A)
- LMWH and non-aspirin antiplatelet drugs are associated with an increased risk of bleeding (except dipyridamole) (A); these should be discontinued in the setting of acute GI bleeding. (C)
- The decision to discontinue these drugs must balance the bleeding risk against the risk of a thromboembolic event. (C)
- For low-risk procedures, these drugs may be continued. (C)
- For high-risk procedures, LMWH should be discontinued at least 8 hours before the procedure. (C)

- For clopidogrel or ticlopidine, there are insufficient data, but, if discontinued, the drug should be withheld for 7 to 10 days. (C)
- Dipyridamole may be continued. (C)
- LMWH may be used as a bridge before endoscopy in patients who require anticoagulation in whom warfarin cannot be safely discontinued. (C)
- LMWH should not be used in pregnant women with mechanical prosthetic heart valves. (B)
- In nonpregnant patients with mechanical valves, short-term use appears to be safe (B); however, prospective controlled data are lacking.

Definitions:

Levels of Evidence

A. Prospective controlled trials
B. Observational studies
C. Expert opinion

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Guidelines for the appropriate practice of endoscopy are based on critical review of the available data and expert consensus. When little or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate management of low-molecular-weight heparin (LMWH) and nonaspirin antiplatelet agents for patients undergoing endoscopic procedures.
- Evidence from prospective controlled trials suggests that LMWH and nonaspirin antiplatelet drugs are effective in the prevention and the treatment of thromboembolic disease

POTENTIAL HARMS

- The administration of protamine sulfate can cause severe hypotension and anaphylactoid reactions.
- Low molecular weight heparin (LMWH) and non-aspirin antiplatelet drugs are associated with an increased risk of bleeding (except dipyridamole); these should be discontinued in the setting of acute gastrointestinal bleeding.
- Ticlopidine has more significant side effects than clopidogrel (e.g., severe neutropenia, thrombotic thrombocytopenic purpura).

CONTRAINDICATIONS

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Low molecular weight heparin (LMWH) should not be used in pregnant women with mechanical prosthetic heart valves.

QUALIFYING STATEMENTS

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Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus. Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Zuckerman MJ, Hirota WK, Adler DG, Davila RE, Jacobson BC, Leighton JA, Qureshi WA, Rajan E, Hambrick RD, Fanelli RD, Baron TH, Faigel DO. ASGE guideline: the management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures. Gastrointest Endosc 2005 Feb;61(2):189-94. [56 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Feb

GUIDELINE DEVELOPER(S)

American Society for Gastrointestinal Endoscopy - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society for Gastrointestinal Endoscopy

GUIDELINE COMMITTEE

Standards of Practice Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Douglas O. Faigel, MD (Chair); Todd H. Baron, MD (Vice Chair); Marc J. Zuckerman, MD; William K. Hirota, MD; Douglas G. Adler, MD; Raquel E. Davila, MD; Brian C. Jacobson, MD, MPH; Jonathan A. Leighton, MD; Waqar A. Qureshi, MD; Elizabeth Rajan, MD; R. David Hambrick, RN CGRN (SGNA representative); Robert D. Fanelli, MD, FACS (SAGES representative)

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Society for Gastrointestinal Endoscopy (ASGE) Web site.

Print copies: Available from the American Society for Gastrointestinal Endoscopy, 1520 Kensington Road, Suite 202, Oak Brook, IL 60523

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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